

Abstract No. Chan0130

**Recognition of the Rotavirus mRNA 3' Consensus by an Asymmetric NSP3 Homodimer**

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Beamline(s): X9A

Rotaviruses, the cause of life-threatening diarrhea in humans and cattle, utilize a functional homolog of poly(A) binding protein (PABP) known as nonstructural protein 3 (NSP3) for translation of viral mRNAs. NSP3 binds to viral mRNA 3' consensus sequences and circularizes the mRNA via interactions with eIF4G. The X-ray structure of the NSP3 RNA binding domain bound to a rotaviral mRNA 3' end has been determined. NSP3 is a novel, heart-shaped homodimer with a medial RNA binding cleft. The homodimer is asymmetric, and contains two similar N-terminal segments plus two structurally different C-terminal segments that intertwine to create a tunnel enveloping the mRNA 3' end. Biophysical studies demonstrate high affinity binding leading to increased thermal stability and slow dissociation kinetics, consistent with NSP3 function.